Notice of Allowability	Application No.	Applicant(s)	
	10/730,555	DARWIN ET AL.	
	Examiner	Art Unit	
	William W. Moore	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *the amendment filed 27 April 2007 and the interview conducted 25 May 2007*.

2. ☒ The allowed claim(s) is/are *1,4-6,13,14,16-20 and 103*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Cancel claim 12.

Amend claims 1, 4, 13, 14, and 17 thus:

1. (Amended) A method of treating a prokaryotic pathogen infection in a subject, said method comprising:
inhibiting the proteolytic activity of a proteasomal core protease in a prokaryotic pathogen by administering an inhibitor of a prokaryotic proteasomal core protease to make the prokaryotic pathogen susceptible to antibacterial host defenses of oxidative stress or nitrosative stress,
thereby treating a prokaryotic pathogen infection in the subject.

4. (Amended) The method according to claim 1, wherein the prokaryotic proteasomal core protease is a product of either the *prc*A gene or the *prc*B gene.

13. (Amended) The method according to claim 1 ~~12~~, wherein the host defense ~~oxidative/nitrosative stress~~ is reactive nitrogen intermediate-induced stress.

14. (Amended) The method according to claim 1 ~~12~~, wherein the host defense ~~oxidative/nitrosative stress~~ is reactive oxygen intermediate-induced stress.

17. (Amended) The method according to claim 1, wherein the inhibitor of prokaryotic proteasomal core protease activity is selected from the group consisting of epoxomicin and N-[4-morpholine]carbonyl-13-[1-naphthyl]-L-alanine-L-leucine boronic acid.

Authorization for this examiner's amendment was given in a telephone interview with Mr. Michael L. Goldman on 25 May 2007.

The following is an examiner's statement of reasons for allowance:

Claim 1 is amended above to introduce the limitations of claim 12 as qualifications of "host defense". Claim 12 is canceled. The term "prokaryotic" is inserted in claims 4 and 17 in view of their dependency from claim 1 and claims 13 and 14 are amended to depend directly from claim 1 and to simplify their recitations. The claimed subject matter is free of the prior art of record where there is no suggestion that compounds capable of inhibiting the activity of prokaryotic proteasome core proteases should be administered to a subject to treat an infection caused by a prokaryotic pathogen. The closest prior art of record herein instead teaches away from a

claimed invention in its disclosure of positive, anti-arthritic, treatment results in simulated infections where mammalian, not prokaryotic, proteasome core proteases are inhibited in order to reduce antigen-mediated T-cell activation in rodents suffering an arthritic response to co-administered staphylococcal and streptococcal antigens. No live prokaryotic pathogen was involved in the co-administration of both prokaryotic antigens and proteasome inhibitors capable of suppressing proteasomal proteolytic activity in the rodent macrophages required for the presentation of pathogen peptide antigens by host MHC molecules. See, Palombello et al., disclosing administration of lactacystin and peptide aldehyde inhibitors, and Zollner et al., disclosing administration of the lactacystin-based compound PS-519.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 571.272.0933 and whose FAX number is 571.273.0933. The examiner can normally be reached Monday through Friday between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Primary Examiner, Dr. Kathleen Kerr, can be reached at 571.272.0931. The official FAX number for all communications for the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.

William W. Moore
25 May 2007

/Nashed/
Nashaat T. Nashed, Ph.D.
Primary Examiner